UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/757,958	11/25/96	WEINER	

EXAMINER

ART UNIT	PAPER NUMBER
1203	33

1203/0123

ALISA A HARBIN
INTELLECTUAL PROPERTY-R440
CHIRON CORPORATION
4560 HORTON STREET
EMERYVILLE CA 94608-2916

DATE MAILED: 01/28/97

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 11/25/96

☒ This action is FINAL.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 O.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-39 is/are pending in the application.
Of the above, claim(s) 13-39 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 1-12 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

-SEE OFFICE ACTION ON THE FOLLOWING PAGES-

* U.S. GPO: 1996-404-496/40517

15. The restriction requirement enunciated in paragraphs 15-20 of the Office Action mailed 8/15/94 is maintained. Applicant's election of Group I, claims 1-12 in Paper No. 23 was acknowledged in paragraph 15 of the Office Action mailed 1/26/95. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election in Paper no. 23 was treated as an election without traverse (M.P.E.P. § 818.03(a)) in paragraph 15 of the Office Action mailed 1/26/95. Claims 13-39 were withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected inventions in paragraph 16 of the Office Action mailed 1/26/95. Election was made without traverse in Paper No. 23.

16. Claims 1-12 are under consideration..

17 The use of the trademarks TRITON X-100, TWEEN 80, SPAN 85, MILLI Q, SEPHADEX PD10, SEP-PAKS AND BRANSON 2000 has been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

18. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

The specification is objected to for the reasons discussed in paragraph 18, sections A-E of the Office Action mailed 7/24/96.

19. Claims 1-12 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth

in the objection to the specification. Applicants arguments have been considered and deemed not persuasive.

Regarding section A, the following comments are made. The specification does not disclose how to use the instant invention for the treatment of HCV infection in humans. Regarding applicants comments on pages 5-9 of the amendment filed 5/6/96, the rejection as elucidated in the previous Office Action provides detailed reasons as to why it would be unpredictable based on the teachings of the specification as to whether the claimed antibodies could be used for the treatment of HCV in vivo in humans. Regarding the four points that applicant lists on page 8 of the instant amendment, the following comments are made. Regarding points one and two, while the specification identifies a conserved motif in the HCV E2/NS1 region and discloses production of antibodies against said region, there is no evidence in the specification that any amino acid sequence encompassed by the peptide recited in the claims is immunogenic or that any antibody produced against any particular peptide encompassed by the formula recited in the claims would bind any other peptide encompassed by the formula recited in the claims. The evidence of record has not demonstrated that any particular antibody preparation against any of the particular amino acid sequences recited in the claims could be used for treating HCV infection in humans. Applicants comments in the letter received 1/25/94 in the instant application indicates that the formula recited in the claims encompasses a minimum of 56,000 different peptides (see page 3, first paragraph). Applicants have provided no evidence that any particular antibody against any of these peptides can be used to treat HCV infection in any individual infected with any isolate of HCV. Weincr et al. (1992) teach that antibodies against a peptide containing a peptide recited in the claims (eg. Q1) which was derived from an HCV infected individual, does not bind a second isolate (Q3) from the same patient which contains a different E2HV peptide than the original isolate, while said second peptide contains a peptide recited in the claims (page 3471, first paragraph). The peptide recited in the claims is at positions 401-406 or 407 of HCV E2HV region, while the peptide disclosed by Weiner et al. is from 396 to 407 of HCV E2HV region (eg. it contains the peptide recited in the claim and therefore contains the antigenic determinant encoded by said peptide). Therefore, it seems unlikely that antibodies against any particular peptide recited in said claims would bind any particular HCV isolate other than a strain with the same amino acid sequence as used to prepare said antibody. There is no disclosure in the specification that the antibody used to treat HCV can only be used

if binds the same peptide as expressed by the strain of HCV to be treated. In addition, applicant has provided no evidence that all of the at least 56,000 peptides encompassed by the formula recited in the claims are immunogenic, and can result in the production of antibodies which bind any strain of HCV. Weiner et al. teaches that patients infected with HCV strains that contain the amino acids encompassed by the formula recited in said claim do not necessarily produce antibodies against said amino acids (eg. see Figure 2). There is simply no disclosure in the specification as to how many peptides encompassed by the claimed formula would be immunogenic and how many would not be immunogenic (eg. could not be used to produce antibodies). It appears that undue experimentation would be required of one skilled in the art to practice the instant invention using the teaching of the specification.

Regarding point three on page 8 of the amendment filed 5/6/96 and applicants comments on page 9 and 10 of the instant amendment, the specification has provided no evidence that any peptide other than the 30-mer peptide disclosed in Example 3 of the specification can be used to produce the antibody used to treat the chimpanzee treated in Example 3 in the specification. The specification has not identified the putative immunoprotective epitope recognized by the antibodies raised against the intact 30-mer peptide. The claims of the instant invention do not read on any antibody which binds the 30mer peptide per se. The specification has provided no evidence to whether said epitope is linear or conformational. Therefore it is unclear as to what region of E2HV could be used an immunogen to produce the antibodies used to treat HCV infection other than the intact 30-mer. Regarding the 30-mer peptide used to immunize the sheep to produce the peptide used in Example 3, page 31 of the specification, the specification discloses that in the two sheep immunized, none of the sheep produce antibodies which bind the 6mer peptide recited in the claims (see page 31, lines 1-6). One of the sheep immunized does produce antibodies which bind a 7mer encompassed by the 7mer peptide recited in the claims (see page 31, lines 1-6). However, with regards to the antibodies used in Example 3 in the specification, there is no disclosure as to what HCV peptides are bound by that IgG preparation (see page 37, penultimate paragraph). All that is disclosed is that the antibodies were derived from sheep immunized with a 30mer peptide from E2HV. There is no disclosure that said antibodies contain antibodies that have the specificity recited for the claimed antibodies. As mentioned above, the specification discloses that sheep immunized with the 30mer can produce antibodies which are not the antibodies recited in the claim. Even in the one shcep that was immunized with the 30mer and

produced an antibody which binds the 7mer encompassed by the 7mer peptide recited in the claims (see page 31, lines 1-6), said sheep also produces antibodies which bind peptides not encompassed by the peptide recited in the instant claims (eg. VSLLA). Therefore, even though the specification does not disclose that antibodies used in Example 3 bound a 7mer as per recited in claims which recite a 7mer, even if this was disclosed in the specification, because the antibody mixture contains antibodies reactive with peptides not encompassed by the peptides recited in the claims it would be unclear as whether the effect seen in Example 3 was the result of the antibodies recited in the claims or antibodies not encompassed by the claims of the instant invention. Furthermore, for the reasons mentioned in the previous paragraph, it appears that any particular antibody encompassed by the claim invention would not bind any and all HCV strains. There is no guidance in the specification as to determine which particular antibody encompassed by the claimed formula can used to treat any particular strain of HCV. Regarding point 4, the claims of the instant invention read on an in vivo method of treatment.

Regarding applicants comments on page 9-11 of the instant amendment, there was no requirement for human data listed in the rejection as elucidated in the previous Office Action. Regarding applicants comments on page 9, the chimpanzee experiment disclosed in Example 3 does not demonstrate that it is predictable that the claimed invention can be used in vivo for the treatment of HCV in humans for the reasons elaborated in the previous two paragraphs. In addition, the specification discloses on page 43, last line, that the serum protein thyroid binding globulin (TBG) binds to "two minimum epitopes, one of which encompasses the SLF--G motif.". The "SLF--G motif" refers to the motif encompassed by the peptides bound by the claimed antibodies. It would therefore be expected that HCV present in human serum would have TBG bound to the SLF--G motif, and therefore said peptide structure would not bc available to bind the exogenously administered antibodies. Regarding applicants request for evidence pursuant to 37 CFR § 1.107(b) on page 11, of the instant amendment, the rejection is supported by evidence as per Weiner et al. and experimental data derived from the specification. Regarding the chimpanzee model in Example 3, there is no data available which indicates whether chimp TBG would bind the SLF--G motif. If the chimp TBG does not bind the TBG, then the chimp model would not be predictive of humans, because it would lack a potential mechanism present in humans that could interfere with binding of HCV antibodies to HCV containing the SLF--G peptide. Regarding the Weiner declaration received 5/6/96, the following comments are made.

Regarding the Choo et al. publication referred to in the Weiner declaration, there is no disclosure in said publication that the chimp model is predictive for antibody mediated therapy of HCV in humans. Said publication deals with immunization with peptides, not antibodies. Furthermore, nowhere in said publication is it disclosed that results obtained in the chimp model predict that a therapeutic agent which works in the chimp model will work in humans. While the chimp model may be used by researchers, there is no evidence of record that it predicts that a particular agent can be used in humans for the treatment of HCV infection. The Choo et al. reference actually seems to state that human and chimps respond in a different immunologic fashion to the same antigen (see page 1295, see first incomplete paragraph, last two sentences). Regarding comments in the Weiner declaration about the chimp experiment disclosed in Example 3 of the specification, the question is not whether antibodies against the 30mer peptide provided protection against HCV in the chimp used, but whether the antibodies recited in the claims would also provide similar protection. It is unclear whether the data in Example 3 of the specification demonstrates that the claimed antibodies can be used to treat HCV infection in humans for the reasons already stated in this rejection.

Regarding applicants analysis of In re Brana, 34 USPQ2d 1436, 1442 (CAFC 1995) on page 10, of the instant amendment, the chimp model disclosed in Example 3 of the specification does not provide evidence that the claimed method can be used for treating HCV infection for the reasons already recited in this rejection. Regarding applicants various comments about the Utility guidelines, no rejection under 35 U.S.C. § 101 is present in the instant application.

Regarding applicants comments on pages 12 and 13, HCV and HIV are both viral diseases that have not been successfully treated in humans using passive immunization. Regarding applicants request for evidence pursuant to 37 CFR § 1.107(b) on page 12, of the instant amendment, the rejection is supported as disclosed in the previous paragraphs. Regarding applicants comments on page 13 of the instant amendment, the claims read on a method of treating HCV infection, not a method of preventing HCV infection in an individual that is not yet HCV infected. Applicants arguments are irrelevant to the claims that are under consideration.

Regarding section B, applicants have provided no evidence that any particular antibody preparation against any of the particular amino acid sequences recited in claims 1-5 could be used in the method of the instant invention. Applicants comments in the letter received 1/25/94

indicates that the formula recited in claims 1 and 2 encompasses a minimum of 56,000 different peptides (see page 3, first paragraph). Applicants have provided no evidence that any particular antibody against any of these peptides can be used to treat HCV infection in any individual infected with any isolate of HCV. Weiner et al. (1992) teach that antibodies against a peptide encompassing the peptide recited in claims 1 and 2 which was derived from an HCV infected individual, do not bind a second isolate (Q3) from the same patient which contains a different E2HV peptide than the original isolate, while said second peptide is still encompassed by the formula recited in claims 1 and 2 (page 305, first paragraph). Therefore, it seems unlikely that antibodies against any particular peptide recited in said claims would bind any particular HCV isolate other than a strain with the same amino acid sequence as used to prepare said antibody. In addition, applicant has provided no evidence that all of the at least 56,000 peptides encompassed by the formula recited in claims 1 and 2 are immunogenic, and can result in the production of antibodies which bind any strain of HCV. There is no evidence disclosed in the specification that the antibodies according to the invention bind to a conserved amino acid region of a large number of isolates. Applicants arguments in this section of the amendment are dependent on facts not elucidated in the specification (eg. antibodies according to the invention bind to a conserved amino acid region of a large number of isolates). Regarding the evidence in Example 1 in the specification, the fact that a variety of different isolates have an alleged conserved peptide as recited in the claims does not provide evidence that any peptide according to the claims will be bound by any antibody made against any peptide recited in the claims. As mentioned above, Weiner et al. indicates that individuals infected with HCV that contains the peptides encompassed by those recited in the claims do not produce antibodies which bind the peptide recited in the claims. Weiner et al. also teaches that a patient which produced an antibody which reacts with a peptide including the peptide recited in the claims does not bind a second peptide which also contains a peptide recited in the claims. As mentioned above, Weiner et al. also teaches that a patient which produced an antibody which reacts with a particular region of E2HV does not bind the same region in a different isolate from the same patient. In view of the fact that it is unclear what peptides recited in the claims would actually give rise to antibodies, and it is unclear as to what percentage of these antibodies would bind any other peptide encompassed by the claims, it appears that undue experimentation would be required of one skilled in the art to practice the instant invention using the teaching of the specification. Regarding applicants comments on pages

14 and 15 of the instant amendment, there is no guidance in the specification as how to determine what peptides encompassed by the claims can or cannot be used to produce antibodies which bind said peptide or any other peptide encompassed by the claims. Weiner et al. disclose that patients exposed to the putative antigenic determinant consisting of the amino acids recited in the claims do not produce antibodies which bind said peptides recited in the claims (see Figure 2). Weiner et al. (1992) teach that antibodies against a peptide containing a peptide recited in the claims (eg. Q1) which was derived from an HCV infected individual, does not bind a second isolate (Q3) from the same patient which contains a different E2HV peptide than the original isolate, while said second peptide contains a peptide recited in the claims (page 3471, first paragraph). Furthermore, the specification discloses that even in sheep immunized with the particular 30mer peptide disclosed in the specification (which contains a amino sequence as recited in the claims)that no antibodies against the 6mer peptide recited in the claims were produced (see page 31, lines 1-6). Furthermore, the specification discloses that no response against the 6mer or 7mer peptide recited in the claims was seen in one of the two sheep immunized with the 30mer peptide.

Regarding section C, applicants have provided no evidence that antibodies against the peptides recited in claims 1-5 can be used in the method of the instant invention. Applicants arguments have been considered and deemed not persuasive. The chimp treated in Example 3, was treated with antibody against a 30-mer peptide. Applicants have provided no evidence that the antibodies that are responsible for whatever putative result was seen upon immunization of said chimp were necessarily derived from the peptides recited in claims 1-5. As applicants point out in the specification (page 13, paragraph four), antibodies recognize epitopes consisting of 3 to 5 amino acids. Applicants have provided no evidence as to the specificity of the antibodies contained in the polyclonal antisera against the 30-mer peptide that are actually responsible for whatever putative result was seen upon immunization of said chimp with said antisera. Regarding applicants comments in the instant amendment on pages 15 and 16, Example 2 in the specification deals with the immune response of goats immunized with a 30-mer peptide.
There is no disclosure in the specification as to which antibodies in the polyclonal antisera against the 30-mer are responsible for whatever result is seen in the single baboon immunized in the single in vivo experiment disclosed in the specification. Furthermore, applicants have provided no evidence that antibodies against the 30-mer do not recognize a conformational epitope not

contained in the peptides recited in claims 1 and 2. Regarding applicants comments on page 15 of the instant amendment, the claimed antibody binds a peptide recited in the claim which encompasses thousands of possible peptides. In paper no. 9 of parent case 08/061,699 (letter received 1/13/94, page 3, last paragraph), applicant estimates that said formula encompasses at least 56,000 sequences. The Weiner et al. reference establishes that not all of these possible peptides can be used to make antibodies. There is no guidance in the specification as to how to determine which of the thousands of peptides encompassed by the peptide recited in the claims can be used to produce the claimed antibodies and which peptides cannot. Regarding applicants comments, there is no disclosure in the specification that the amino acids in positions 4 and 5 of the 6-mer motif are irrelevant. In fact, Figure 2.1 seems to suggest that there is preferential use of certain amino acids (eg. 24/58 sequences contain proline at position five of the 6 mer amino acid motif). There is no data disclosed in the specification indicating what role the amino acids at positions 4 and 5 play in binding of antiHCV antibodies to the sequence recited in the claims. Furthermore, Weiner et al. teaches that a peptides encompassed by the peptides recited in the claims does not even elicit antibodies in an infected individual that is infected with a variant that expresses a E2HV protein of a particular strain (see Abstract). Thus, even if only 140 combinations of critical residues were encompassed by the peptide recited in the claims, there is no disclosure in the specification as to what percentage of these peptides actually bind antiHCV antibodies or are even sufficiently immunogenic that antiHCV antibodies would be elicited in an infected patient, while Weiner et al. teaches that peptides which are encompassed by the peptide recited in claims exist which do not bind antiHCV antibodies.

Regarding section D, applicants have presented no evidence that any peptide other than the 30-mer peptide disclosed in Example 3 of the specification can be used to produce the antibody used in the method of the instant invention and achieve the putative results disclosed in Example 3 in the specification. Applicants arguments have been considered and deemed not persuasive. Applicants have not identified the putative immunoprotective epitope recognized by the antibodies raised against the intact 30-mer peptide. Applicants have no evidence to whether said epitope is linear or conformational. Therefore it is unclear as to what region of E2HV could be used an immunogen to produce the antibodies used in the method of the instant invention other than the intact 30-mer. Regarding the 30-mer peptide used to immunize the sheep to produce the peptide

used in Example 2, page 31 of the specification, the specification discloses that in the two sheep immunized, none of the sheep produce antibodies which bind the 6mer peptide recited in the claims (see page 31, lines 1-6). One of the sheep immunized does produce antibodies which bind a 7mer encompassed by the 7 mer peptide recited in the claims (see page 31, lines 1-6). However, with regards to the antibodies used in Example 3 in the specification, there is no disclosure as to what HCV peptides are bound by that IgG preparation (see page 37, penultimate paragraph). All that is disclosed is that the antibodies were derived from sheep immunized with a 30mer peptide from E2HV. There is no disclosure that said antibodies contain antibodies that have the specificity recited for the claimed antibodies. As mentioned above, the specification discloses that sheep immunized with the 30mer can produce antibodies which are not the antibodies recited in the claim. Even in the one sheep that was immunized with the 30mer and produced an antibody which binds the 7mer encompassed by the peptide recited in claims which recite a 7mer (see page 31, lines 1-6), said sheep also produces antibodies which bind peptides not encompassed by the peptide recited in the instant claims (eg. VSLLA). Therefore, even though the specification does not disclose that antibodies used in Example 3 bound a 7mer as per recited in claims which recite a 7mer, even if this was disclosed in the specification, because the antibody mixture contains antibodies reactive with peptides not encompassed by the peptides recited in the claims it would be unclear as whether the effect seen in Example 3 was the result of the claimed antibodies or antibodies not encompassed the claims of the instant invention.

Regarding section E, applicants have presented no evidence that the antibody used in Example 3 of the specification can be used to prevent HCV when the recipient of the antibody is exposed to any HCV strain other than the strain used in Example 3. It is unclear that the antisera used in Example 3 will bind any HCV strain other than the particular strain used in said experiment. Weiner et al. (1992) teach that antibodies against a peptide encompassing the peptide recited in claims 1 and 2 which was derived from an HCV infected individual, do not bind a second isolate (Q3) from the same patient which contains a different E2HV peptide than the original isolate, while said second peptide is still encompassed by the formula recited in claims 1 and 2 (page 305, first paragraph). Therefore, it seems unlikely that antibodies against any particular peptide recited in said claims would bind any particular HCV isolate other than a strain with the same amino acid sequence as used to prepare said antibody. Regarding applicants comments on page 18, first paragraph, there is no evidence provided in the specification that any

one particular antibody against a peptide recited in the claims binds any other peptide encompassed in the formula. In fact, Weiner et al. teaches the opposite (eg. an antibody against a peptide encompassing the peptide recited in claims 1 and 2 which was derived from an HCV infected individual, does not bind a second isolate (Q3) from the same patient which contains a different E2HV peptide than the original isolate, while said second peptide is still encompassed by the formula recited in claims 1 and 2). Regarding the evidence in Example 1 in the specification, the fact that a variety of different isolates have an alleged conserved peptide as recited in the claims does not provide evidence that any peptide according to the claims will be bound by any antibody made against any peptide recited in the claims. As mentioned above, Weiner et al. also teaches that a patient which produced an antibody which reacts with a particular region of E2HV does not bind the same region in a different isolate from the same patient. In view of the fact that it is unclear what peptides recited in the claims would actually give rise to antibodies, and it is unclear as to what percentage of these antibodies would bind any other peptide encompassed by the claims, it appears that undue experimentation would be required of one skilled in the art to practice the instant invention using the teaching of the specification. There is no guidance in the specification as how to determine what peptides encompassed by the claims can or cannot be used to produce antibodies which bind said peptide or any other peptide encompassed by the claims.

20. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

21. Claims 1-12 remain rejected under 35 U.S.C. § 103 as being unpatentable over Ralston et al. (WO 92/08734) in view of Houghton et al.(WO 90/11089) for the reasons elaborated in the previous Office Action. Applicants arguments have been considered and deemed not persuasive. Ralston et al. teach that regarding the E2 antigen (which contains the conserved amino acid sequence recited in claim 1) that, "Immunogenic compositions may be administered to animals to induce production of antibodies, either to provide a source of antibodies or to induce protective immunity in the animal." (page 15, lines 15-19). The animal immunized with intact E2 antigen would produce a polyclonal antisera containing antibodies against any and all immunogenic epitopes expressed on said molecule (eg. including the conserved motif recited in claim 1). Claim 1 as currently written reads on a method using an antibody composition "comprising" an antibody capable of binding to a conserved amino acid. Therefore, the mixture of antibodies as produced by immunization with E2 antigen which contains antibodies against the conserved amino acid sequence recited in claim 1 would constitute prior art, because the claim as currently written does not read on a composition which only contains antibodies against the conserved amino acid sequence recited in the claims. Regarding the use of term "substantially isolated", because the claim reads on an antibody composition, said composition can contain other antibodies.

22. No claim is allowed.

23. This application is a FWC of applicant's earlier Application No. 08/061699. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will

the statutory period for response expire later than SIX MONTHS from the date of this final action.

24. Since the fee set forth in 37 CFR 1.17(r) for a first submission subsequent to a final rejection has been previously paid, applicant, under 37 CFR 1.129(a), is entitled to have a second submission entered and considered on the merits if, prior to abandonment, the second submission and the fee set forth in 37 CFR 1.17(r) are filed prior to the filing of an appeal brief under 37 CFR 1.192. Upon the timely filing of a second submission and the appropriate fee of $730.00 for a large entity under 37 CFR 1.17(r), the finality of the previous Office action will be withdrawn. In view of 35 U.S.C. 132, no amendment considered as a result of payment of the fee set forth in 37 CFR 1.17(r) may introduce new matter into the disclosure of the application.

25. Papers related to this application may be submitted to Group 180 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Papers should be faxed to Group 180 at (703) 305-7939.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Ron Schwadron whose telephone number is (703) 308-4680. The examiner can normally be reached Tuesday through Friday from 8:30 to 6:00.
The examiner can also be reached on alternative Mondays. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 180 receptionist whose telephone number is (703) 308-0196.

RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP 1800

R Schwadron

Ron Schwadron, Ph.D.
Primary Examiner
Art Unit 1816
January 24, 1997